Allergic Rhinoconjunctivitis

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Introduction

- Definition
- Epidemiology
- Classification
- Symptoms
- Conjunctivitis
- Associated diseases and risk factors
- Pathophysiology
- Evaluation and differential diagnosis
- Treatment

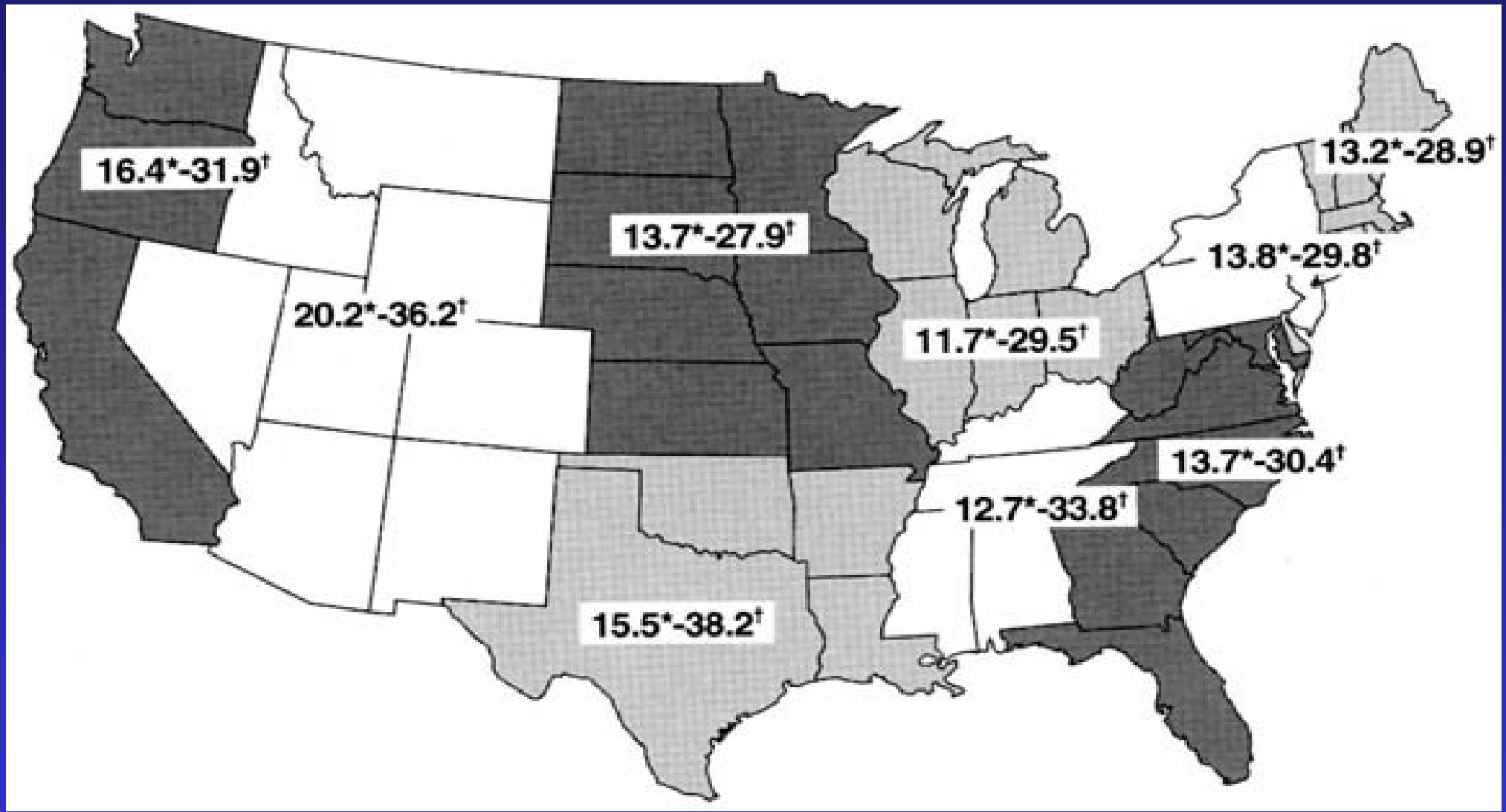
Definition

- Inflammation of the membranes lining the nose
- Characterized by
  - nasal congestion
  - rhinorrhea
  - sneezing
  - itching of the nose
  - postnasal drainage
- IgE-mediated reaction to a specific aeroallergen

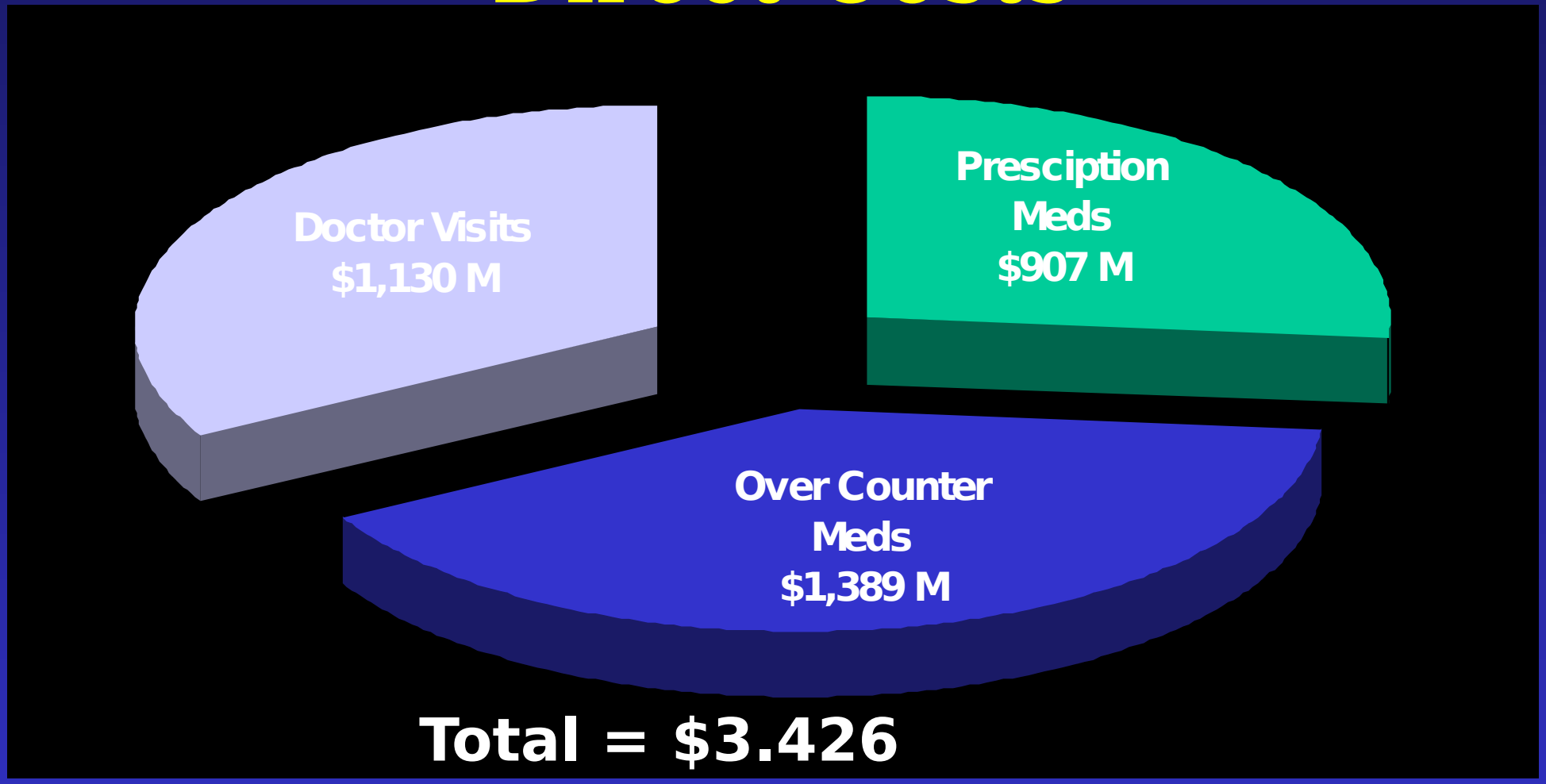
Epidemiology

- 10-25% of population (peak 14-25 yrs. old)
  - 30-50 million Americans
  - 3.5 million work days and 2 million school days missed
  - Cost >$5 billion annually
- 80% develop symptoms before age 20
  - 20% have sx by 2-3 yrs of age
  - 40% have sx by 6 yrs of age
  - Boys > Girls in childhood; equal ratio in adulthood

Prevalence by Region



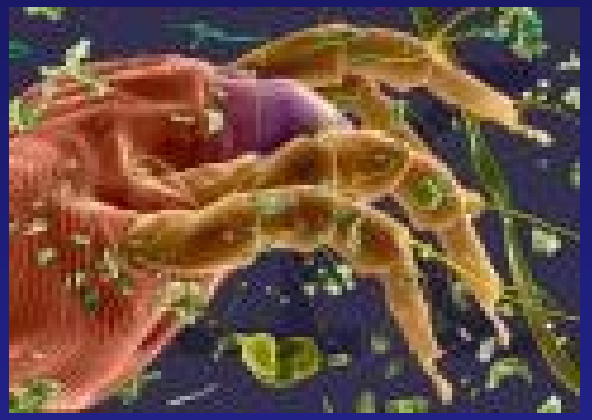
Direct Costs



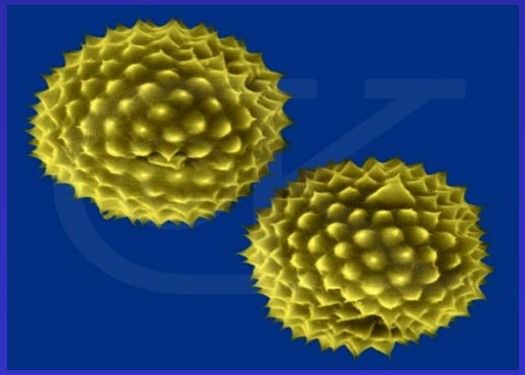
Total = $3.426 Billions

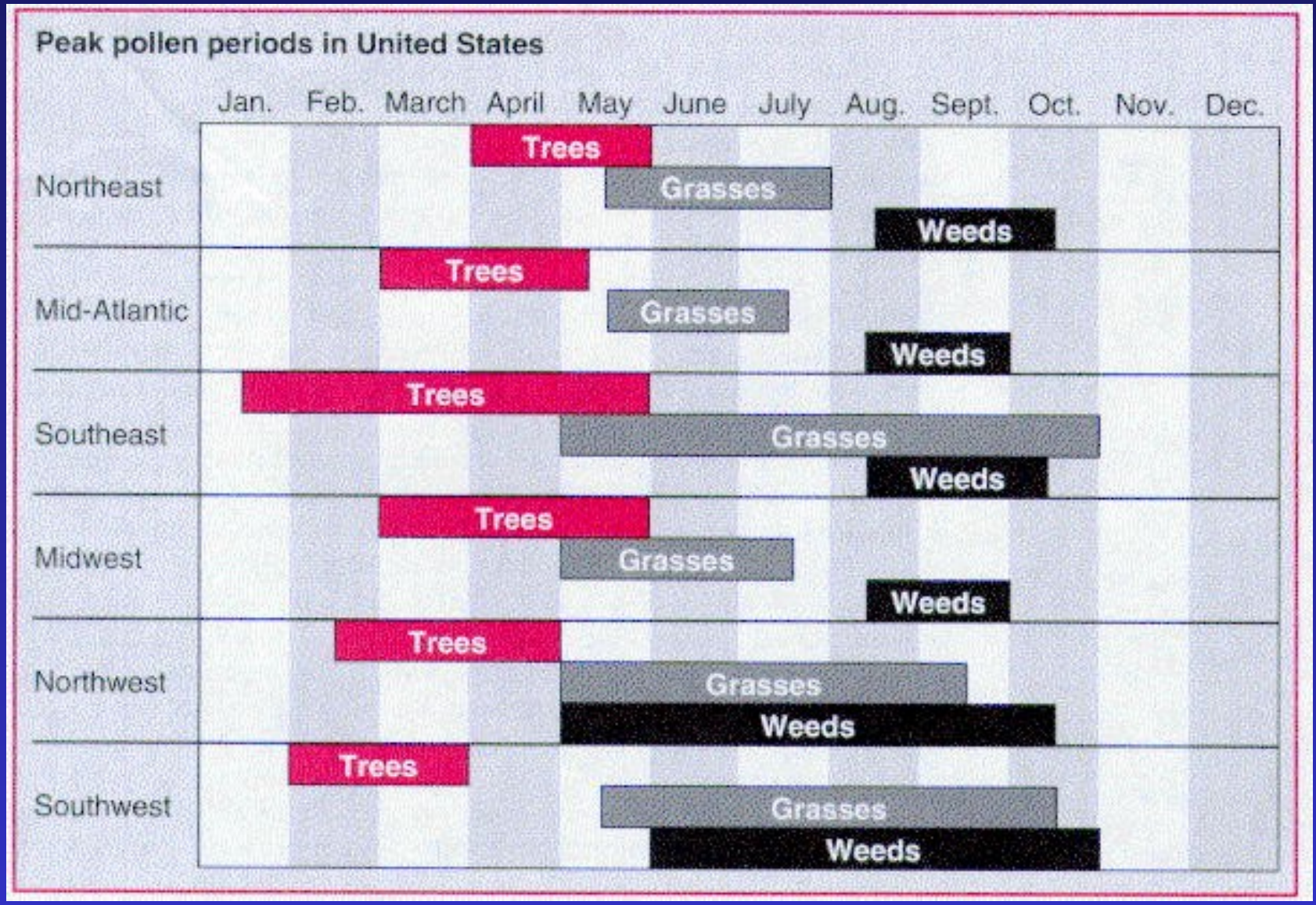
Storms et al. JACI 1997;99:s820-4.

Classification

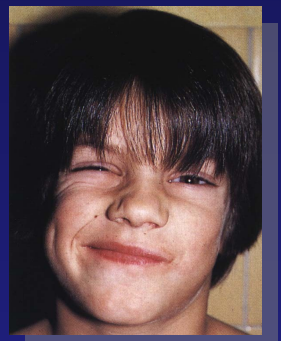


- Perennial
  - Most common cause is the dust mite
  - Other frequent causes include pets, cockroaches, molds
- Seasonal
  - Symptoms for a limited period, recurring each year
- Occupational
  - latex, lab animals,…

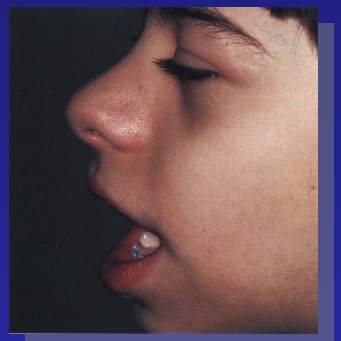


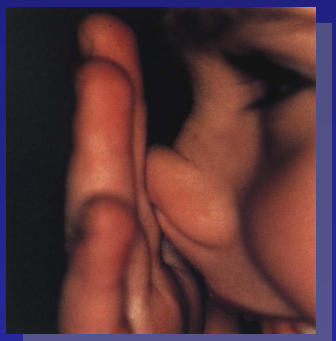

Peak pollen periods in United States
Jan.
Feb.
March
April
May
June
July
Aug.
Sept.
Oct.
Nov.
Dec.
Northeast
Trees
Grasses
Weeds
Mid-Atlantic
Trees
Grasses
Weeds
Southeast
Trees
Grasses
Weeds
Midwest
Trees
Grasses
Weeds
Northwest
Trees
Grasses
Weeds
Southwest
Trees
Grasses
Weeds

Symptoms



- Sneezing
- Rhinorrhea (clear)
- Nasal congestion
- Nasal and/or ocular pruritis
- Red eyes
- Increased lacrimation—white, stringy exu
- Itching of palate, eustachian tube, inner e
- Post nasal drip
- Dry cough





Up to 30% of patients will only have ocular symptoms

Risk Factors of AR

- Increased risk with
  - family history of allergic disorder (maternal > paternal)
  - *maternal* smoking ≥ 1 pack of cigarette/day (in first year of life)
  - firstborn, or born during pollen season
  - early introduction of foods and formula
  - higher socioeconomic class
  - nonwhite
  - high serum IgE levels (>100 IU/ml before age 6)

Allergic Rhinitis & Associated Diseases

- Otitis media and sinusitis
  - Increased incidence with allergic rhinitis
  - Impaired mucocilliary clearance and tissue edema
- Asthma
  - 80-90% of asthmatics have AR; 15% of AR have asthma
  - United Airways Disease (UAD)
    - allergic rhinitis represents an early stage of UAD
    - nasal challenge can elicit bronchi contraction or ↑bronchial responsiveness (naso-bronchial reflex)

Allergic Rhinitis: Pathophysiology

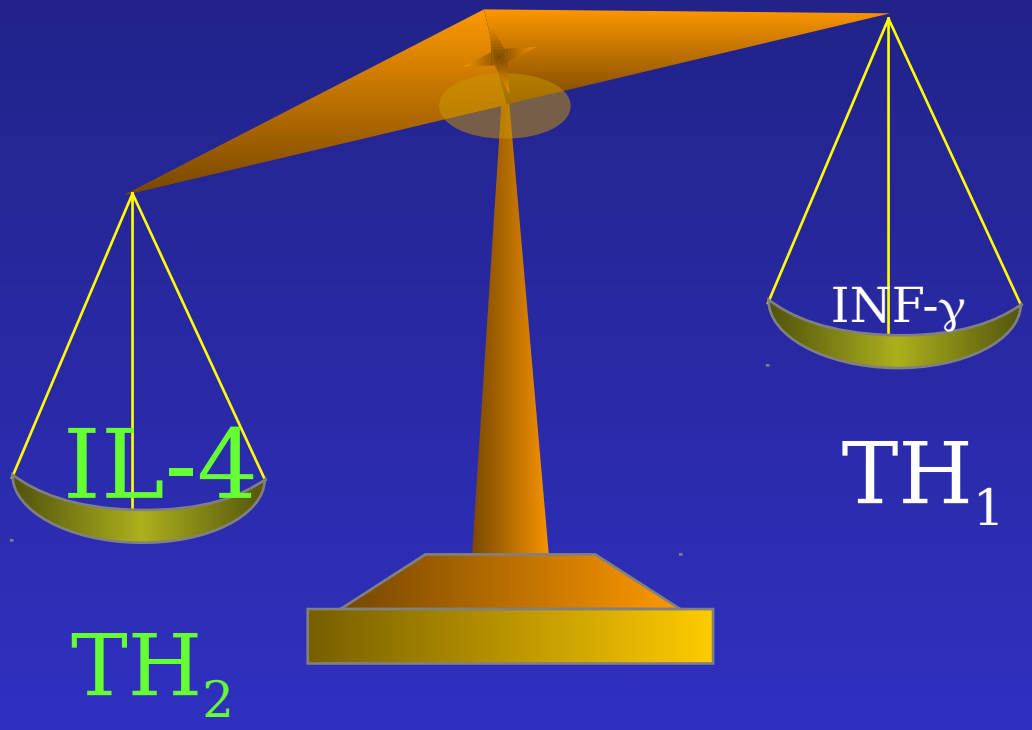
off the mark
by Mark Parisi
www.offthemark.com
LISTEN GUYS...AS THE BODY'S NATURAL DEFENSE SYSTEM, WE'RE ALWAYS SO DARN SERIOUS! WHADAYA SAY WE DO SOMETHING WACKY? LET'S OVER-REACT TO SOMETHING HARMLESS LIKE PEANUT BUTTER OR POLLEN!
YEAH!
comics.com
HOW ALLERGIES START

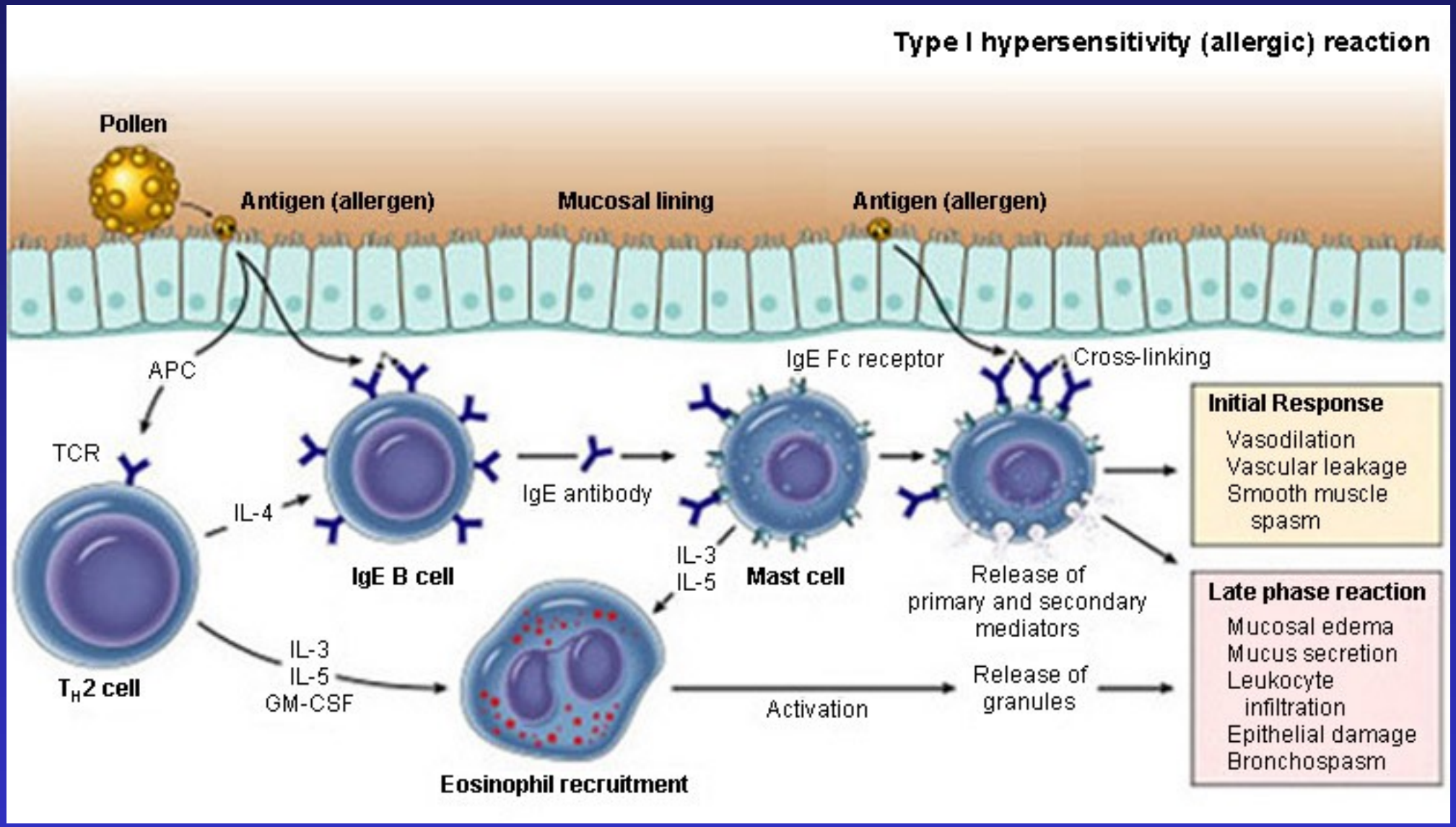
Allergic Rhinitis: Pathophysiology

Inflammatory disorder driven by T_H2 lymphocytes

→ 3 steps

1. Sensitization
2. Early response
3. Late response




Type I hypersensitivity (allergic) reaction
Pollen
Antigen (allergen)
Mucosal lining
Antigen (allergen)
APC
TCR
IL-4
IgE B cell
IgE antibody
IgE Fc receptor
Cross-linking
IL-3
IL-5
Mast cell
Initial Response
Vasodilation
Vascular leakage
Smooth muscle spasm
Release of primary and secondary mediators
Late phase reaction
Mucosal edema
Mucus secretion
Leukocyte infiltration
Epithelial damage
Bronchospasm
T_H2 cell
IL-3
IL-5
GM-CSF
Activation
Release of granules
Eosinophil recruitment

Diagnosis

- Suggestive history
- Supportive exam
- Specific IgE-identif

History

- Symptoms
  - Onset
  - Seasonal vs. perennial
  - Triggers (cat, smoke, food, odors…)
- Family history

Physical Exam

- General appearance and vital sign
- Eyes - conjunctiva, lid eversion
- Ears
- Nares
  - Mucosa
    - Color
    - Bogginess/edema
    - Cobblestoning
  - Secretions
  - Septum

Physical Findings

Allergic shiner - dark swollen, infraorbital tissue
Allergic salute - transverse crease across nasal brid

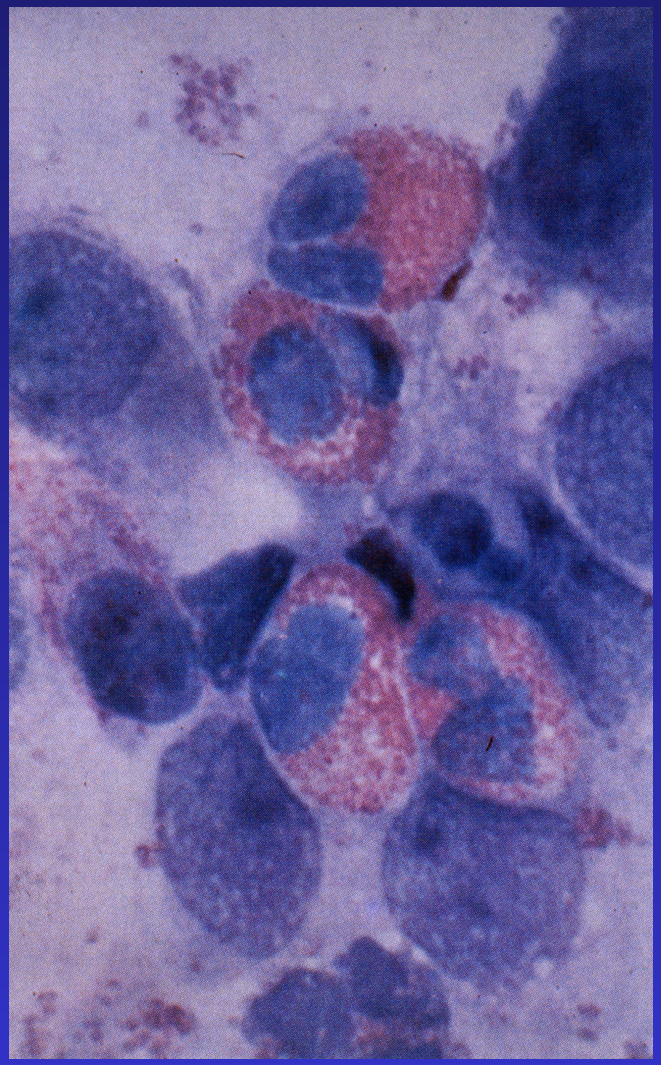
Physical Exam

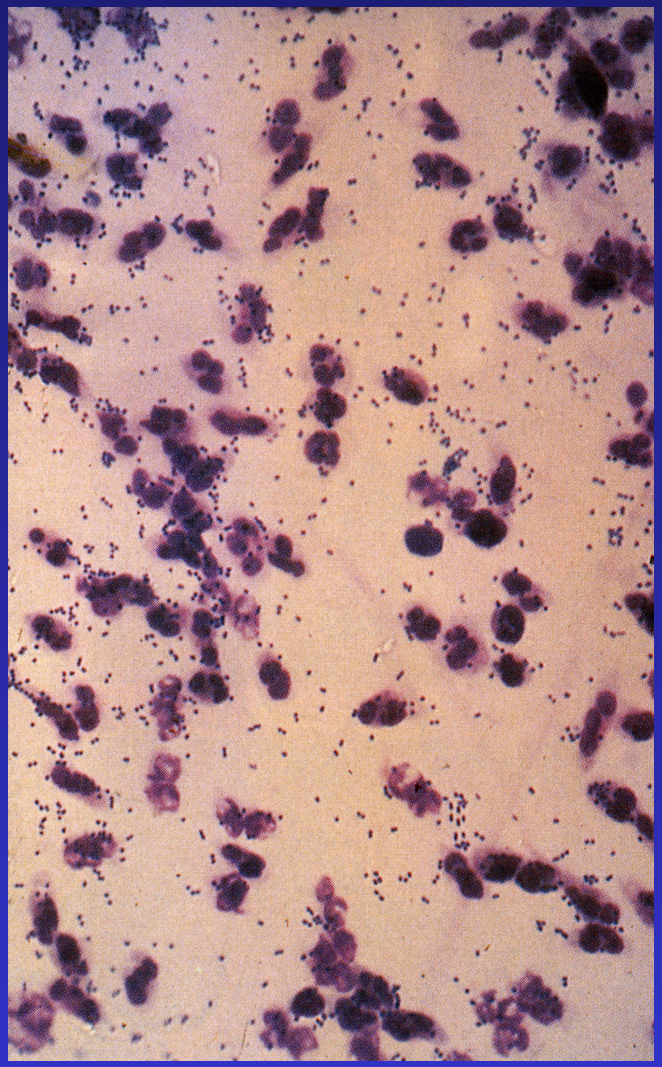
- Oropharynx
  - post-nasal drip, cobblestoning
- Neck
  - adenopathy, stridor
- Lungs
  - wheezing
- Heart
- Skin
  - eczema, urticaria

Nasal Cytology

- May help differentiate allergic rhinitis from infection
- Perform Wright's or Hansel's stain
- NARES (non allergic rhinitis with eosinophilia syndrome)

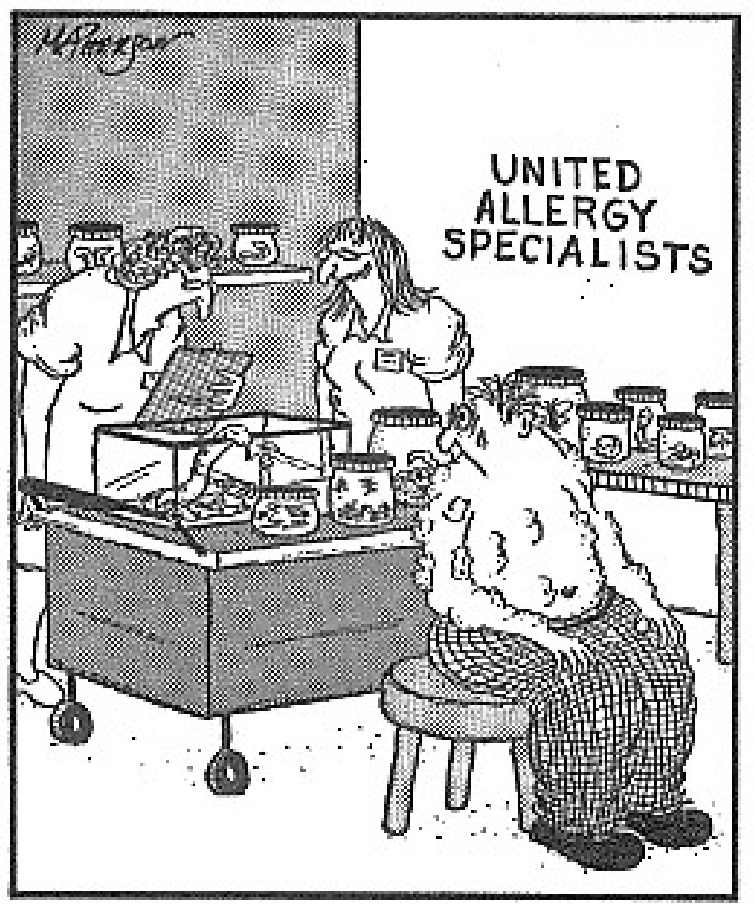
Nasal Smears





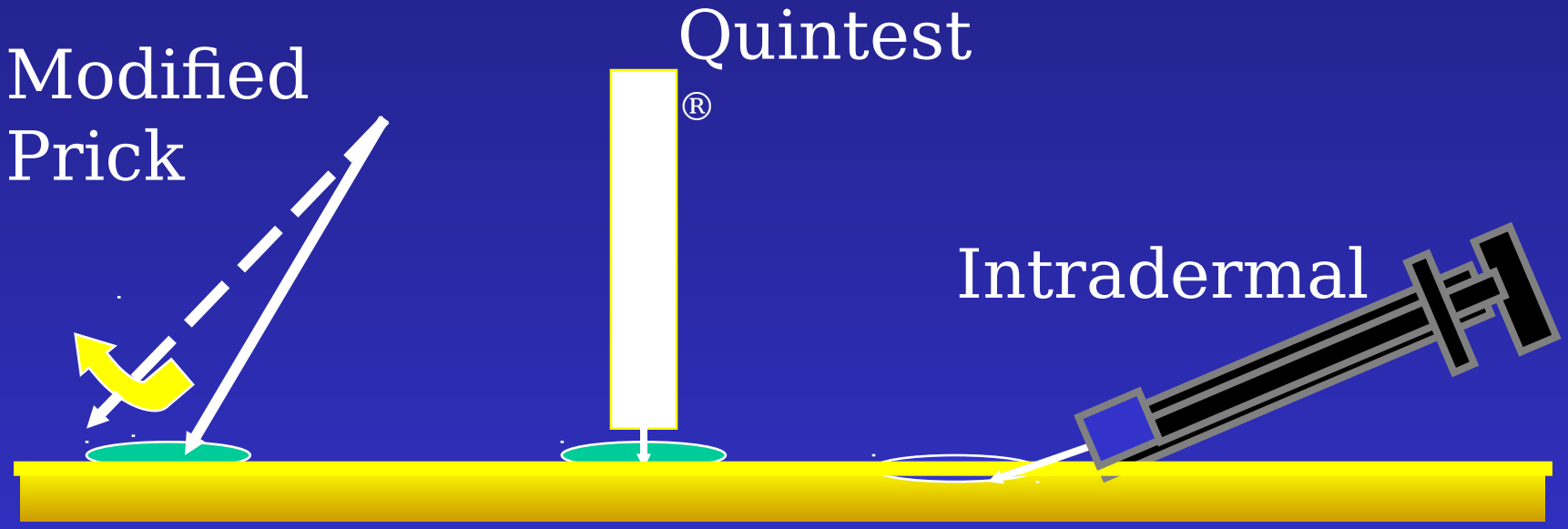
Allergy Testing

- Skin testing
  - prick
  - intradermal
- Serum testing
  - RAST



"Well, let's see. He's positive for hay fever, negative for mildew, positive for poison ivy, positive for bee stings, positive for poison sumac. Let's see how he does with the fire ants."

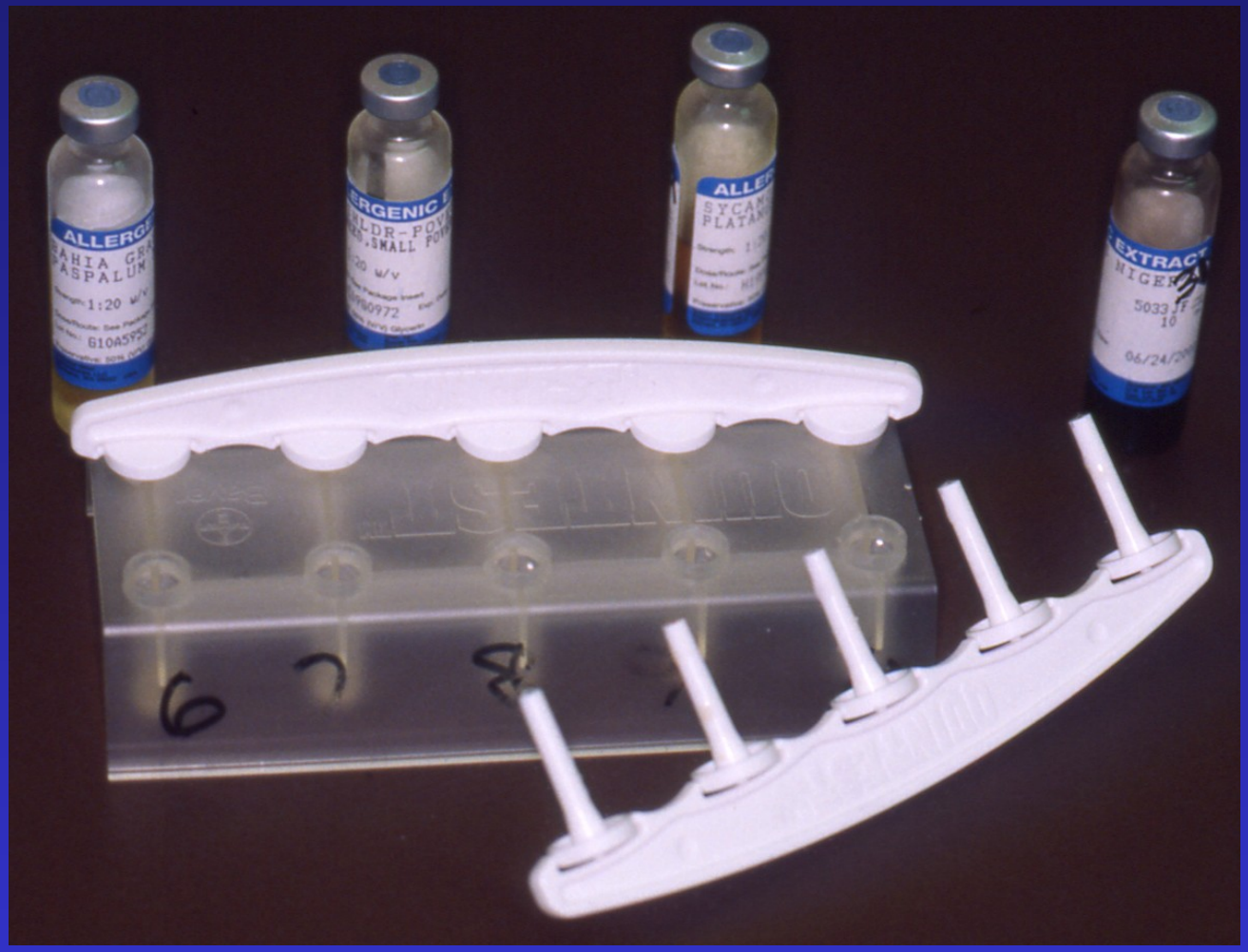
Skin Testing



Prick Skin Testing

- Benefits
  - cheap
  - very sensitive and specific (most specific allergy test)
  - wide selection of allergens for testing
  - rapid results
- Drawbacks
  - suppressed by antihistamines
  - small chance of allergic reaction during test
- Always test with positive (histamine) and negative (saline) controls

Skin Testing Method



Skin Testing Technique

Skin test results

Intradermal Skin Testing

- Subcutaneous injection of allergen
- Traditionally used when increased sensitivity is needed
- More sensitive than prick
- But much less specific
  - many false positives
- Increased risk of severe reaction

Drugs that interfere with skin testing

- False negatives
  - Antihistamines
    - discontinue 5-7 days prior to testing
  - Antidepressants with antihistamine activity
    - amitriptyline, nortryptiline, etc
- Increased risks
  - Beta blockers
    - relative contraindication
    - WHMC does not perform skin test if patient on beta-blockers
  - ACE Inhibitors
    - theoretical risk
    - not currently a contraindication at WHMC

Radioallergosorbent Test (RAST)

- Measurement of serum IgE specific for allergen
  - does not measure IgE actually bound to mast cells
- Indicated for patients with skin conditions
  - eczema or dermatographism
- Or for patients who can’t stop their medications
  - beta blockers or antihistamines
- Not suppressed by antihistamines
- No anaphylactic risk to the patient

Radioallergosorbent Test (RAST)

- Drawbacks
  - Less sensitive?
  - Less specific
  - Smaller selection of allergens to choose from
  - More expensive
    - $112 for a 21 allergen panel

RAST

Class	*IgE* *(kU/L)*	*Level of Antigen*
0	<0.35	Absent/undetectable
1	0.35-0.70	Low
2	0.71-3.50	Moderate
3	3.51-17.5	High
4	17.6-50.0	Very high
5	51-100	Very high
6	>100	Very high

Differential Diagnosis: *Nonallergic rhinitis*

- Inflammatory
- Non-inflammatory
- Structural

Inflammatory NAR

- Infections
  - bacterial or viral URI's
- Nasal polyps
- Nasal/systemic immunologic disease
  - Wegener's, sarcoidosis, SLE, Churg-Strauss
- Nonallergic rhinitis with eosinophilia syndrome (NARES)
  - perennial symptoms
  - nasal eosinophilia
  - negative skin test or RAST

Non Inflammatory NAR

- Metabolic
  - Pregnancy, OCP's, hypothyroidism, acromegaly
- Vasomotor
  - Irritants (strong smells, smoke, exhausts, temperature variation)
  - Cold air
  - Bright lights
  - Gustatory (hot & spicy foods, alcohol)
- Emotional factors
  - autonomic stimulation with stress or sexual arousal
- Medications
  - Rhinitis medicamentosa
  - Antihypertensives

Rhinitis Medicamentosa

- Most commonly from overuse of topical decongestants (eg., Afrin)
  - Chronic nasal obstruction and inflammatory hypertrophy of the nasal mucosa
- >5-7 days of use leads to tachyphylaxis and rebound *congestion* on withdrawal
- Nasal mucosa classically appears “beefy red”
  - Can usually see areas of punctate bleeding
- Treatment requires stopping the offending agent
  - nasal steroids can help reduce inflammation
  - occasionally oral steroids are used during withdrawal

Antihypertensives Causing NAR

Trade Name	Generic	Symptoms
Aldomet*	Methyldopate	Nasal stuffiness
Apresoline†	Hydralazine	Nasal congestion, dyspnea
Cardura‡	Doxazosin	Nasal congestion
Catapres§	Clonidine	Dryness of nasal mucosa
Corgard¶	Nadolol	Nasal stuffiness, bronchospasm, cough
Hytrin**	Terazosin	Nasal congestion
Ismelin†	Guanethidine	Dyspnea, asthma in susceptible individuals, nasal congestion
Minipress‡	Prazosin	Nasal congestion, dyspnea
Moduretic*	Amiloride and hydrochlorothiazide	1% nasal congestion, 1% dryness
Normodyne††	Labetalol	Nasal stuffiness, wheezing in 1
Trandate‡‡	Labetalol	Nasal stuffiness, dyspnea, bronchospasm
Wytensin§§	Guanabenz	Nasal stuffiness, dyspnea
—	Reserpine	Nasal congestion, dyspnea

Annals of Allergy, Asthma, and Immunology May 2001

Structurally-related NAR

- Septal deviation
- Enlarged or deformed turbinate
- Adenoidal hypertrophy (esp. in children)
- Neoplastic/non-neoplastic tumors
- Foreign body
- CSF leakage
  - copious watery, unilateral discharge, s/p trauma (95% within 3 months), surgery, or neoplasm
  - ✓ glucose concentration or β2-transferrin

Allergic vs Nonallergic

- Sneezing
- Clear, watery discharge
- Pruritus
- Nasal congestion
- Post nasal drip
- Cough
- Hoarseness
- Headache
- Sinusitis

} Think Allergy

Treatment

- Environmental control
- Medications
  - Nasal steroids
  - Antihistamines
  - Mast cell stabilizer
  - Decongestants
  - Anticholinergics
  - Leukotriene modifiers
- Immunotherapy

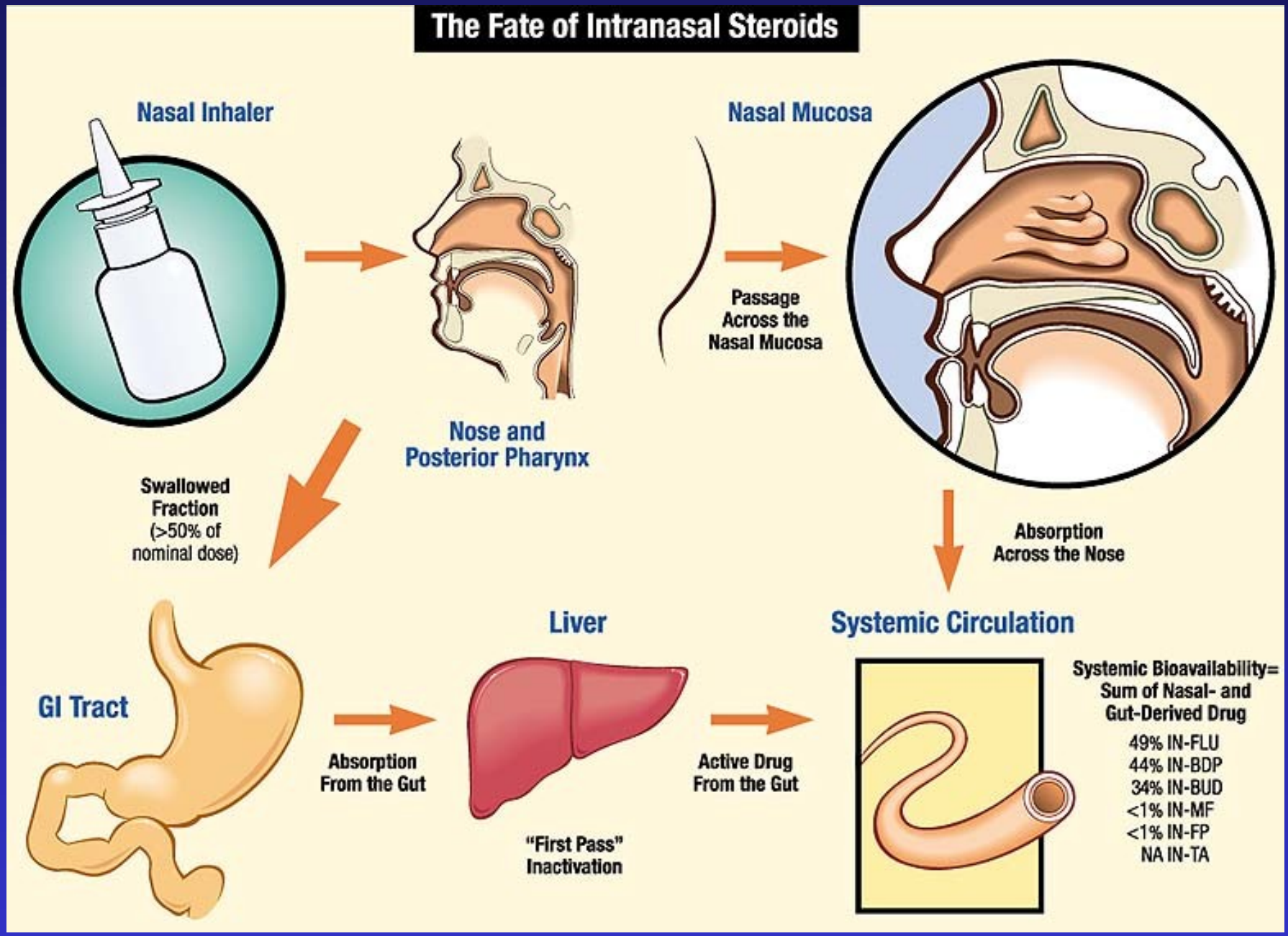
Nasal Corticosteroi

- Anti-inflammatory
  - shrink nasal polyps and mucosa
- Effective in >90% of patients
- Better sx control than any other monotherapy
- Slow onset; daily use required
- Side effects:
  - dry nasal mucosa, epistaxis, septal perforation (rare)
  - no affect on adrenocortical function
  - case reports of ↑ intraocular pressure
  - ? growth suppression

Nasal Corticosteroids

		FDA Approved
Beclomethasone	Vancenase, Beconase	≥ 6 years old
Triamcinolone	Nasacort	≥ 6 years old
Budesonide	Rhinocort	≥ 6 years old
Fluticasone	Flonase	≥ 4 years old
Mometasone	Nasonex	≥ 2 years old

- may take up to 2 weeks for full effects to occur
- side effects: stinging/burning, epistaxis, sneezing, & nasal septal perforation


The Fate of Intranasal Steroids
Nasal Inhaler
Nasal Mucosa
Passage Across the Nasal Mucosa
Nose and Posterior Pharynx
Swallowed Fraction (>50% of nominal dose)
Absorption Across the Nose
GI Tract
Liver
Systemic Circulation
Absorption From the Gut
"First Pass" Inactivation
Active Drug From the Gut
Systemic Bioavailability= Sum of Nasal- and Gut-Derived Drug
49% IN-FLU
44% IN-BDP
34% IN-BUD
<1% IN-MF
<1% IN-FP
NA IN-TA

Antihistamines

- Effective in reducing itching, sneezing, and rhinorrhea
- First line therapy for treatment of allergic rhinitis
- Little effect on nasal congestion
- Reduce symptoms of allergic conjunctivitis

Antihistamines

- 1st generation
  - Lipophilic → sedation
  - Impairment in reaction time, coordination, and learning…even without sx of sedation
  - Anticholinergic side effects (watch out in elderly)
    - Dry mouth, dry eyes, urinary retention
- 2nd generation
  - Reduced sedation
  - Typically effective over 24 hours (qday dosing)
- Work best as maintenance therapy
  - Will not displace histamine from receptor

2nd Generation Antihistamines

Low-sedating			
Cetirizine	Zyrtec	12 & up	10 mg
		6-11 years	5-10 mg
		1-5 years	2.5-5 mg
		6-12 mos	2.5 mg
Non-sedating			
Fexofenadine	Allegra	12 & up	180 mg
		6-11 years	30 mg bid
Loratadine	Claritin	6 & up	10 mg
		2-5 years	5 mg

Nasal antihistamine

Azelastine (Astelin)

- intranasal antihistamine spray used twice a day
- 10x more potent than chlorpheniramine at the H_1 receptor
- rapid onset (2-3 hours)
- significantly less sedation (11%) and anticholinergic effects
- bitter taste
- FDA-approved for allergic and nonallergic rhinitis

Mast Cell Stabilizer

- Cromolyn sodium (Nasalcrom)
  - Decreases release of mast cell mediators
  - Safe
  - Not as effective as antihistamines or steroids (only effective PRIOR to allergen exposure)
  - Dosing 4-6 x/day for optimal response

Decongestants

- Oral
  - Pseudoephedrine (Sudafed)
  - Compounded with Allegra, Claritin and Zyrtec
  - May cause tachycardia and hypertension
  - Phenylpropanolamine removed from market (↑ CVA risk)
- Topical
  - Oxymetazoline (Afrin)
  - Phenylephrine (Neo-synephrine)
  - Instant gratification
  - Rhinitis medicamentosa with chronic use (>3-5 days)

Ipratropium Bromide

- Atrovent nasal spray
  - topical anti-cholinergic
  - best for secretory/rhinorrhea symptoms
- Short acting
- Few side effects (nasal drying, minor epistaxis)
- Indications and dosing
  - Children ages 6 and up (2 sprays bid-tid)
  - Non-allergic rhinitis (*chronic use*) 0.03%
  - Rhinovirus infections (*short-term use*) 0.06%

Comparison of agents

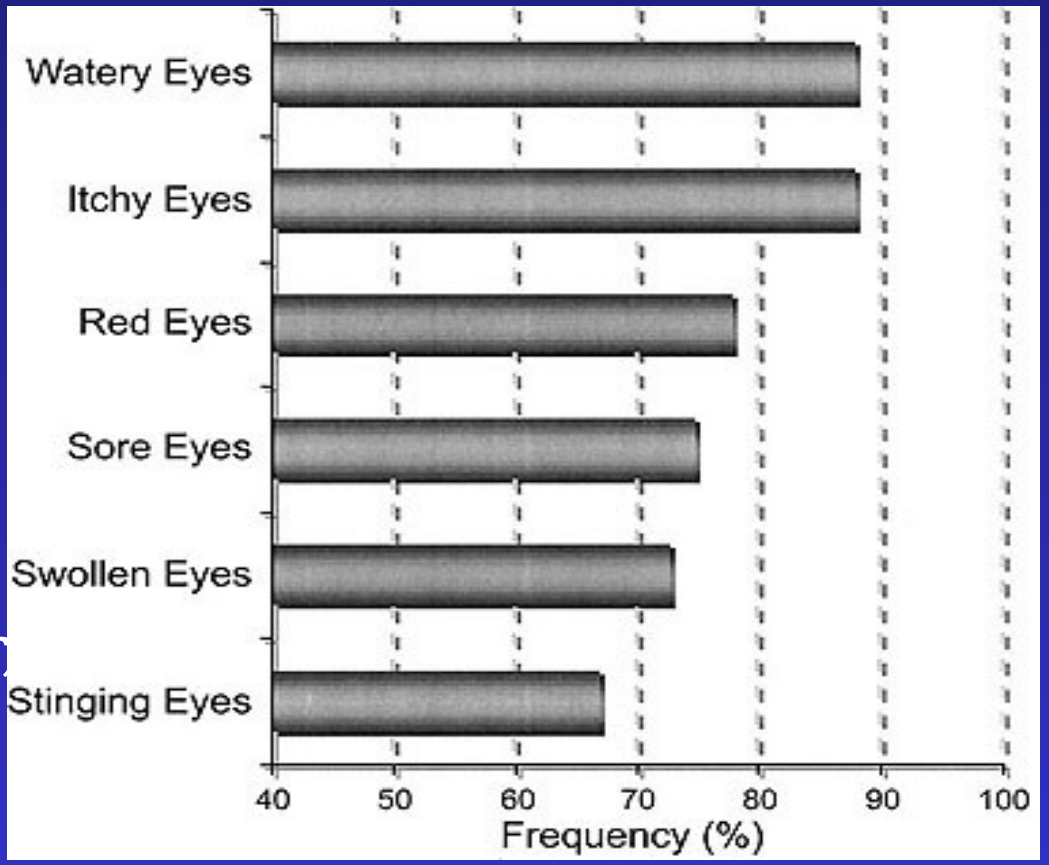
Agent	*Sneezing*	*Itching*	*Congestion*	*Eye Symptoms*	*Rhinorrhea*
Oral Antihistamine	**++**	**++**	**+/–**	**++**	**++**
Nasal Antihistamine	**+**	**+**	**+/–**	**+**	**+/–**
Intranasal Corticosteroid	**++**	**++**	**++**	**++**	**+**
Oral Decongestant	**–**	**–**	**+**	**–**	**–**
Intranasal Decongestant	**–**	**–**	**++**		

Allergies And The Eye

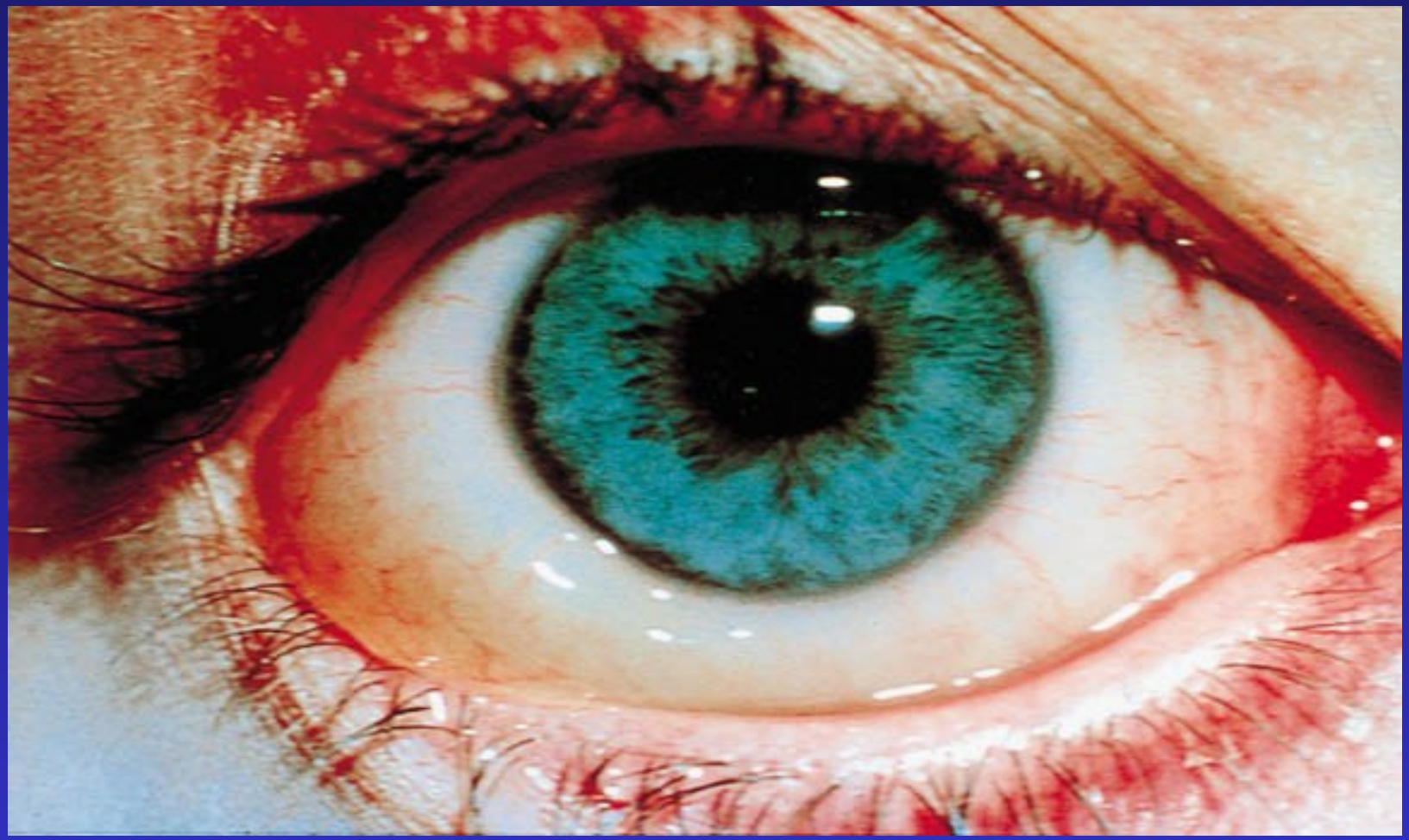
1. Allergic conjunctivitis
2. Atopic keratoconjuctivitis
3. Vernal keratoconjunctivitis

Allergic Conjunctivitis

- Seasonal (SAC)
  - 50% of allergic conjunctivitis
  - grass most common offender
- Perennial (PAC)
  - Dust mites, animal dander, feather



Chemosis of the conjunctiva



As seen in allergic conjunctivitis

Atopic Keratoconjunctivitis

- Chronic inflammation of the eye
- Begins in late teens to early 20’s
- Associated with atopic dermatitis (95%) and asthma (85%)
- Can lead to (anterior) cataracts and blindness (corneal scarring)
- Sx: itching, burning, tearing (worse than SAC/PAC)
- Trantas dots

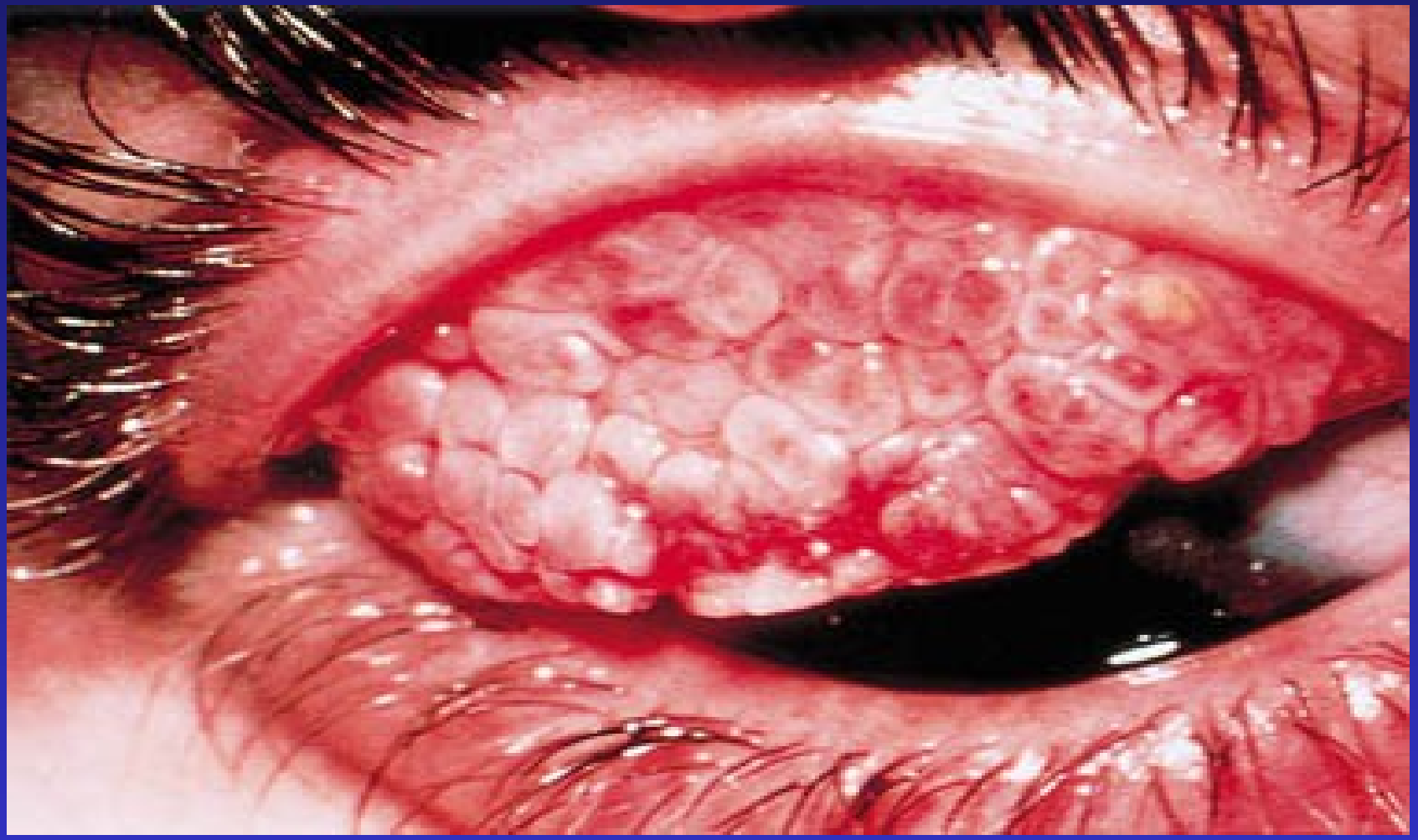
Vernal Keratoconjunctivitis

- Severe bilateral recurrent inflammation
- Marked seasonal incidence (frequent onset in spring)
- Onset in children and young adults (with h/o asthma, eczema)
  - typically outgrown by adulthood
- May cause blindness if involves cornea
- Sx: intense pruritis (↑ with wind, light, heat), photophobia, foreign body sensation, lacrimation
- Signs: milk colored fibrinous secretion, corneal shield ulcers, cobblestone papillae, Trantras dots

Trantras dots

Discrete swellings with white dots, indicating degenerating cellular debris
Seen in atopic keratoconjunctivitis and vernal conjunctivitis

Cobblestoning



Giant papillae on upper tarsal plate, as seen in vernal keratoconjunctivitis

Ocular Allergy Therapy

- **Lodoxamine** (Alomide)
  - mast cell stabilizer
  - 2500 x potency of cromolyn sodium
  - slow onset of action
  - 1-2 gtts qid
- **Olopatadine HCL** (Patanol)
  - H-1 antigonist/histamine release inhibitor
  - very effective ⇒ rapid relief of pruritis and erythema
  - expensive
  - safe down to age 3
  - 1 gtts bid (improved compliance)
- **Ketotifen fumarate** (Zaditor)
  - similar to Patanol

Ocular Allergy Therapy

- **Artificial tears**
  - safe and cheap
  - minimally effective
- **Naphazoline** (Naphcon, Vasacon)
  - H-1 antagonist/decongestant combo
  - effective and rapid relief (better than systemic antihistamine)
  - cheap
  - 1-2 gtts bid-qid
  - contraindicated in narrow angle glaucoma
- **Levocabastine HCL** (Livostin)
  - H-1 antagonist
  - effective, but short acting
  - 1-2 gtts qid

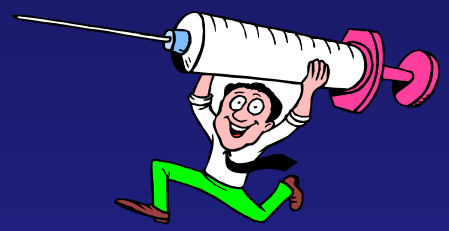
Treatment in Pregnancy

- **Antihistamines**
  - CTM, Benadryl, Zyrtec, Claritin (Cat B)
  - Allegra, Astelin, Atarax, Clarinex (Cat C)
- **Decongestants**
  - Pseudoephedrine (Cat C)
  - Allegra-D and Zyrtec-D are Cat C
  - but Claritin-D is Cat B
- **Nasal steroids**
  - all Cat C
  - except budesonide (Rhinocort - Cat B)
  - beclomethasone (Beconase) is Cat C but has long history of safety
- Atrovent nasal spray
  - Cat B
- Singulair
  - Cat B

Treatment in Pregnancy

Eye Drops	
Cromolyn	B
Alomide	B
Patanol	C
Zaditor	C
Livostin	C

Immunotherapy



- Highly effective!
- Indicated if failed medical therapy
- Need 3-5 year time commitment from patient
- Risks of systemic reactions
  - qualified personnel
  - watch patient for 30 minutes
  - crash cart available
  - treat with epinephrine